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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/879,329	06/12/2001	Ethan R. Signer	408445	4053

23557 7590 08/01/2007

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EXAMINER	
SULLIVAN, DANIEL M	
ART UNIT	**PAPER NUMBER**
1636	

MAIL DATE	DELIVERY MODE
08/01/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/879,329	SIGNER ET AL.	
	Examiner	Art Unit	
	Daniel M. Sullivan	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 May 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16 and 18-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *8,9,19 and 20* is/are allowed.

6)☒ Claim(s) *1-7,10-16,18 and 21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is a response to the Paper filed 15 May 2007 in response to the Final Office Action mailed 15 December 2006. Claims 1-16 and 18-21 were considered in the 15 December Office Action. Claims 1 and 4 were amended in the 15 May Paper. Claims 1-16 and 18-21 are pending and under consideration.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 15 May 2007 has been entered.

Response to Amendment and Arguments

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various

claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 4, 6, 10, 12, 14, 15 and 18 **stand rejected** under 35 U.S.C. 103(a) as being unpatentable over Bauer *et al.* and further in view of Ow, D. (WO 93/01283) for reasons of record and herein below in the response to Applicant arguments.

As described in the 1 April 2004 Office Action, Bauer *et al.* teaches a genetic construct comprising a positive selectable marker gene and a negative selectable marker gene, different in kind from the positive selectable marker, and direct repeats of a gene of interest that flank the positive and negative selectable marker genes (see especially the paragraph beginning at line 34 in column 3 and the paragraph bridging columns 3-4). With regard to the limitation of the substrate as "complementary to" the selectable marker, Applicant indicates that this relationship is described in paragraph 30 of the specification. Based on the description therein, the limitation is understood to encompass any medium or growth condition that provides for selection by the marker gene. In columns 8-10, Bauer *et al.* contemplates a variety of positive and negative selectable marker genes and media or growth conditions that provide for selection (*e.g.*, inducers of promoters operably linked to nucleic acids encoding toxic gene products for use as negative selectable markers).

Furthermore, in the paragraph bridging columns 10-11, Bauer *et al.* teaches a method of removing a selectable marker comprising transforming cells with the genetic construct disclosed

therein, identifying transformants using the integration marker (*i.e.*, positive selection marker) and then selecting cells that have lost the negative selection marker by culturing in negative selection medium. Thus, Bauer *et al.* teaches a genetic construct having all of the limitations of the genetic construct system of the instant claim 1 and a method having all of the limitations of claim 4 except that Bauer *et al.* does not teach the construct system applied to plants.

Ow teaches a method of producing marker-free transgenic plants wherein a selectable marker gene is flanked by site specific recombination sites and excised using a site specific recombinase (see especially the discussion beginning the first full paragraph on page 6 and continued through the first full paragraph on page 7).

It would have been obvious to one of ordinary skill in the art to substitute the method of Bauer *et al.*, using a construct comprising a positive and negative selectable marker flanked by direct repeats according to the instant claims, for the method of Ow, which utilizes a selectable marker flanked by site specific recombination signals to remove selectable marker genes from plant cells. One would be motivated to modify the teachings of Ow in this way in view of the teaching of Bauer *et al.* that site specific recombination systems are inferior to the method disclosed therein because the site specific recombination does not remove all of the exogenous DNA (see especially column 3, lines 26-28).

Absent evidence to the contrary, one would have a reasonable expectation of success in practicing the method of Bauer *et al.* in plant cells because one of ordinary skill would expect that the homologous recombination required for deletion of the marker genes would operate in plant cells as well as yeast.

In view of these considerations, the instant claims 1 and 4, as a whole, would have been obvious to one of ordinary skill in the art at the time the invention was made, as would the method of claim 17, which merely recites that the eukaryotic cell is a plant cell.

Finally, claim 18, which limits the cell of claim 17 to one of a variety of species, would also be obvious to one of ordinary skill in the art because Ow teaches that excision of marker genes is generally desirable in any transgenic plant (see especially the third paragraph on page 4) and explicitly contemplates production of marker-free tobacco (see especially Example 2).

For these reasons, the invention of claims 1, 4, 17 and 18 as a whole would be obvious to one of ordinary skill in the art at the time of filing.

With regard to claims 6, 10, 12, 14 and 15, the claims are directed to the genetic construct of claim 1, wherein the positive and negative selectable markers are limited to specific arrangement within the construct with respect to one another (*e.g.*, GI-PS-NS-GI *versus* GI-NS-PS-GI). Claims 14 and 15 are further limited to comprising additional genes of interest flanking the gene of interest present as a direct repeat. As originally discussed in the 1 April Office Action (page 5), although Bauer *et al.* does not explicitly teach any particular configuration of the positive and negative selectable markers, other than that they should be flanked by the direct repeat, the skilled artisan would not expect that the arrangement of the selectable markers within the boundaries of the direct repeat would affect the function of the construct in any way.

A *prima facie* case of obviousness may be made when chemical compounds have very close structural similarities and similar utilities because one skilled in the art would be motivated by the expectation that compounds of similar structure will have similar function (see *e.g.*, MPEP 2144.09). Thus, it would be *prima facie* obvious to the skilled artisan to use either of the

configurations of positive and negative selectable markers set forth in the claims. With regard to additional genes of interest, Bauer *et al.* teaches that the constructs might comprise one or several additional genes of interest located outside of the direct repeat sequence (see especially column 4, lines 11-14).

Given these teachings, the invention of claims 6, 10, 12, 14 and 15, as a whole, would also have been obvious to one of ordinary skill in the art at the time the invention was made.

Response to Arguments

In response to the *prima facie* rejection and arguments of record, Applicant has amended the claims such that each direct repeat of the gene of interest comprises "a nucleic acid sequence encoding a peptide". Applicant contends that the difference between the present invention and Bauer is that Bauer requires that the direct repeat sequences and is not translated to from a peptide. Applicant admits that Bauer indicates that it is possible to use a fragment of a gene that encodes a protein as a DRS but contends that this teaching does not render obvious what is claimed because Bauer teaches that efforts should be made to prevent the gene fragment from being translated into the form of a peptide.

This argument has been fully considered but is not deemed persuasive. The argument appears to be based on the assumption that the claims require that the construct be configured such that a peptide is expressed from the direct repeats. However, the claims require only that the genetic construct comprise direct repeats that "encode a peptide". According to the broadest reasonable construction of "encode a peptide" the direct repeats need only encode two or more

consecutive amino acids. The claims do not require that the peptide actually be expressed from the direct repeats; it must only be encoded by the direct repeats.

As Applicant acknowledges in the remarks, Bauer teaches that it is possible to use a fragment of a gene as a direct repeat sequence. (Page 8, first full paragraph, of the 11 October Paper.) In fact, Bauer teaches that the DRS can contain portions of protein encoding genes. (Column 7, first full paragraph.) Therefore, Bauer does teach that, in one embodiment, the DRS might be of a gene of interest that encodes a protein. Furthermore, Bauer teaches that the DRS sequence will contain from 80 to 300 bp. Given that the claim only requires that the DRS encode a sequence of two or more consecutive amino acids and Bauer teaches using portions of protein coding genes containing from 80-300 bp, it would be obvious a DRS would comprising at least one sequence encoding a peptide because portions of protein coding genes containing from 80-300 bp that do not encode at least one peptide would be extremely rare and difficult to find.

Applicant's arguments have been fully considered but are not deemed persuasive in view of the record as a whole. Therefore, the claims stand rejected under 35 U.S.C.§103 as obvious over the art.

New Grounds

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 2, 3, 5, 7, 11, 13, 16 and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bauer *et al.* (*supra*) and further in view of Ow (*supra*) as previously applied to claims 1, 4, 6, 10, 12 and 14, and further in view of Lassner et al. US Pub No. 2002/0035739 A1.

As described in the 1 April 2004 Office Action, Bauer *et al.* teaches a genetic construct comprising a positive selectable marker gene and a negative selectable marker gene, different in kind from the positive selectable marker, and direct repeats of a gene of interest that flank the positive and negative selectable marker genes (see especially the paragraph beginning at line 34 in column 3 and the paragraph bridging columns 3-4). With regard to the limitation of the substrate as "complementary to" the selectable marker, Applicant indicates that this relationship is described in paragraph 30 of the specification. Based on the description therein, the limitation is understood to encompass any medium or growth condition that provides for selection by the marker gene. In columns 8-10, Bauer *et al.* contemplates a variety of positive and negative selectable marker genes and media or growth conditions that provide for selection (*e.g.*, inducers of promoters operably linked to nucleic acids encoding toxic gene products for use as negative selectable markers).

Furthermore, in the paragraph bridging columns 10-11, Bauer *et al.* teaches a method of removing a selectable marker comprising transforming cells with the genetic construct disclosed therein, identifying transformants using the integration marker (*i.e.*, positive selection marker) and then selecting cells that have lost the negative selection marker by culturing in negative selection medium. Thus, Bauer *et al.* teaches a genetic construct having all of the limitations of the genetic construct system of the instant claim 1 and a method having all of the limitations of claim 4 except that Bauer *et al.* does not teach the construct system applied to plants.

Ow teaches a method of producing marker-free transgenic plants wherein a selectable marker gene is flanked by site specific recombination sites and excised using a site specific recombinase (see especially the discussion beginning the first full paragraph on page 6 and continued through the first full paragraph on page 7).

It would have been obvious to one of ordinary skill in the art to substitute the method of Bauer *et al.*, using a construct comprising a positive and negative selectable marker flanked by direct repeats according to the instant claims, for the method of Ow, which utilizes a selectable marker flanked by site specific recombination signals to remove selectable marker genes from plant cells. One would be motivated to modify the teachings of Ow in this way in view of the teaching of Bauer *et al.* that site specific recombination systems are inferior to the method disclosed therein because the site specific recombination does not remove all of the exogenous DNA (see especially column 3, lines 26-28).

Absent evidence to the contrary, one would have a reasonable expectation of success in practicing the method of Bauer *et al.* in plant cells because one of ordinary skill would expect

that the homologous recombination required for deletion of the marker genes would operate in plant cells as well as yeast.

In view of these considerations, the instant claims 1 and 4, as a whole, would have been obvious to one of ordinary skill in the art at the time the invention was made.

With regard to claims 6, 10, 12 and 14, the claims are directed to the genetic construct of claim 1, wherein the positive and negative selectable markers are limited to specific arrangement within the construct with respect to one another (*e.g.*, GI-PS-NS-GI *versus* GI-NS-PS-GI). Claims 14 and 15 are further limited to comprising additional genes of interest flanking the gene of interest present as a direct repeat. As originally discussed in the 1 April Office Action (page 5), although Bauer *et al.* does not explicitly teach any particular configuration of the positive and negative selectable markers, other than that they should be flanked by the direct repeat, the skilled artisan would not expect that the arrangement of the selectable markers within the boundaries of the direct repeat would affect the function of the construct in any way.

A *prima facie* case of obviousness may be made when chemical compounds have very close structural similarities and similar utilities because one skilled in the art would be motivated by the expectation that compounds of similar structure will have similar function (see *e.g.*, MPEP 2144.09). Thus, it would be *prima facie* obvious to the skilled artisan to use either of the configurations of positive and negative selectable markers set forth in the claims. With regard to additional genes of interest, Bauer *et al.* teaches that the constructs might comprise one or several additional genes of interest located outside of the direct repeat sequence (see especially column 4, lines 11-14).

Bower et al. and Ow do not teach a negative selectable marker gene that is codA. However, Lassner et al. teaches, "Examples of negatively selectable markers useful in the context of plant genetic engineering include a number of genes involved in herbicide metabolism, including...codA..." (Paragraph 0033.)

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the teachings of Bower et al. and Ow to use codA as the negative selectable marker gene because Lassner et al. teaches that codA is a negatively selectable marker gene that was known in the art to be useful for plant genetic engineering. One would have been motivated to use the codA marker gene and one would have had a reasonable expectation of success in using the codA marker gene in view of the teaching of Lassner et al. that the codA gene was established as an effective negative selectable maker useful in plant genetic engineering. Furthermore, as Ow specifically identifies nptII as a selectable marker that can be used in constructs for plant engineering as contemplated therein (see especially page 7, line 30) the instant claim 30, as a whole, would also have been obvious to one of ordinary skill in the art at the time the invention was made in view of the teachings of the cited art.

In view of the foregoing, the invention of claims 3, 5, 7, 11, 13 and 12, as a whole, would also have been obvious to one of ordinary skill in the art at the time the invention was made. Therefore, the claims are properly rejected under 35 USC § 103(a).

Allowable Subject Matter

Claims 8, 9 and 19-20 are allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel M. Sullivan whose telephone number is 571-272-0779. The examiner can normally be reached on Monday through Friday 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach, Ph.D. can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) (http://pair-direct.uspto.gov) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

/Daniel M. Sullivan/
Primary Examiner
Art Unit 1636